



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JUN 15 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Reregistration of Oxyfluorfen: Time Extension Request; Chemical No. 111601;
Case No. 2490; Branch No. 9913; DP Barcode No. D173513

FROM: Christine L. Olinger, Chemist *Christine L. Olinger*
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THRU: Andrew Rathman, Section Head *Andrew Rathman*
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TO: Mark Wilhite/Bruce Sidwell
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Special Review and Reregistration Division (H7508C)

In a letter dated 4/16/92 Rohm and Haas Company has requested time extensions for several studies required for the reregistration of oxyfluorfen. The registrant states that additional time is required to complete livestock metabolism studies, storage stability, and animal feeding studies which were due in May 1992.

Oxyfluorfen, a List B chemical, is a herbicide for which tolerances are established in/on numerous commodities in 40 CFR 180.381.

RECOMMENDATIONS

The time extensions for which CBRS can recommend are summarized in Table 1. CBRS recognizes that granting of time extensions is within the purview of SRRD.

Based on the preliminary results of the goat and hen metabolism studies, the registrant should address the following concerns in the final report.

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- The registrant should provide a justification for the 170-190% dose recovery in the goat metabolism study.
- The registrant should provide an explanation for the sudden increase in TRR for milk on day 4 of dosing (4-5x increase) with a comparable decrease the following day. This occurred in goats with either the NPR or CPR label.
- The registrant is reminded that tissues, eggs, and milk from the metabolism studies should be analyzed by enforcement and residue data collection methods to ensure that oxyfluorfen residues of concern can be analyzed by these methods.
- Samples from the metabolism studies will be stored for an extended period of time by the time the study has been completed. The registrant should provide data demonstrating that the metabolic profile did not change significantly over the study interval.

Table 1. Recommended Time Extensions for Oxyfluorfen Studies

Study	Registrant Request	CBRS Recommendation
171-4(a) Nature of the Residue - Goat	December 1992	December 1992
171-4(a) Nature of the Residue - Hen	March 1993	December 1992
171-4(e) Storage Stability	December 1994	December 1994
171-4(j) Magnitude of the Residue - Meat, Milk, Poultry, Eggs	March 1994	September 1993

DETAILED CONSIDERATIONS

171-4(a) Nature of the Residue - Goat

Registrant Request

An extension to December 1992 has been requested to complete this study, which was initiated in January 1991. A contract lab conducted the dosing and initial quantitation in early 1991. The tissue samples were not shipped to the registrant until October 1991. Metabolite identification commenced the following month.

Goats were dosed separately with oxyfluorfen ¹⁴C-labeled in two different positions. Approximately 170-190% of the dose was recovered from the tissues, milk, feces, and urine. Parent oxyfluorfen has been found (as the only metabolite) in the milk, fat, and muscle. Confirmation has yet to be conducted in the muscle. Residues in the liver (TRR = 0.17 ppm) and kidney (TRR = 0.052 ppm) appear to be polar and difficulty has been experienced in

identification.

CBRS Comment

CBRS questions why no work was conducted on the study for over six months; if work has continued, the study may have been completed on time. If the preliminary results are valid, Rohm and Haas has made progress toward metabolite identification. CBRS has no reason to object to a time extension on a scientific basis, but acknowledges that granting of time extensions is within the purview of SRRD.

CBRS recommends that the registrant provide an explanation for their unusually high dose recovery (170-190%) in the final report.

171-4(a) Nature of the Residue - Hen

Registrant Request

An extension to March 1993 has been requested for completion of this study. Hens were dosed in January 1991 (separately) with oxyfluorfen ¹⁴C-labeled in two different positions. The samples were shipped to a second contract lab for metabolite characterization.

Preliminary results were presented in the time extension request. A considerable amount of the TRR has already been characterized (Refer to table 2.)

CBRS Comment

In all tissues (except liver) >80% of the TRR has been characterized. Aside from chromatography of fractions which have not been analyzed, CBRS considers the most important work remaining to be identification of Metabolite B, hydrolysis of the liver post-extraction solids, and characterization of the water-soluble residue from the liver. (See shaded areas of table 2.) The registrant should be able to complete this work by the end of December 1992. Work completed to date should be submitted in December 1992. If the registrant considers additional work necessary to delineate the oxyfluorfen residues of concern, then a detailed justification should be provided. CBRS recognizes that granting of time extensions is within the purview of SRRD.

171-4(e) Storage Stability

Registrant Request

The registrant has requested an extension to December 1994 for completion of storage stability studies. Previous studies, which were initiated at Craven Laboratories, were terminated in December 1991. New studies to be initiated this year will require approximately two years to complete.

CBRS Comment

If two years is required to complete the study, then the registrant must have stored magnitude of residue samples for an extended period of time. CBRS has no scientific reason to object to the requested time extension, but acknowledges that granting of a time extension is within the purview of SRRD.

171-4(j) Magnitude of the Residue - Meat, Milk, Poultry, and Eggs**Registrant Request**

Due to delays with the livestock metabolism studies the registrant has requested an extension to March 1994 for completion of magnitude of residue studies.

CBRS Comment

Preliminary results should indicate to the registrant which metabolites should be analyzed in the magnitude of residue studies. There is no reason why the studies could not commence by the end of 1992 and completed within 9 months. CBRS can recommend for an extension to September 1993, but recognizes that granting of a time extension is within the purview of SRRD.

cc: CLOlanger (CBRS), Circulate, List B File, RF, SF
H7509C:CBRS:CLOlanger:clo:CM#2:Rm 805B:305-5406: 6/09/92
RDI: JSSmith: 6/10/92 MMetzger: 6/10/92

Table 2. Preliminary Results of Oxyfluorfen Metabolism Hen Study

	Whole Egg				Thigh Muscle				Breast Muscle			
	CPR ¹		NPR ²		CPR		NPR		CPR		NPR	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Oxyfluorfen	65.9	1.00	57.6	1.15	86.2	1.03	83.7	1.10	76.2	0.14	76.6	0.14
RH-34670 ³	14.6	0.22	20.8	0.42	4.4	0.05	3.8	0.05	5.0	0.01	4.6	0.01
Met. A	--	--	--	--	0.8	0.01	ND	ND	-	-	-	-
Met. B	14.8	0.22	15.8	0.32	1.3	0.02	1.4	0.02	2.3	<0.01	1.0	<0.01
Met. C	--	--	--	--	ND	ND	2.6	0.03	ND	ND	1.4	<0.01
PES ⁴	0.5	0.01	0.9	0.02	1.8	0.02	2.5	0.03	8.9	0.02	9.3	0.02
Identified	80.5	1.22	78.4	1.57	90.6	1.08	87.5	1.15	81.2	0.15	81.2	0.20
TRR	--	1.51	--	2.00	--	1.18	--	1.31	--	0.19	--	0.24

	Liver				Fat/Skin			
	CPR		NPR		CPR		NPR	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Oxyfluorfen	60.8	0.77	64.1	0.84	95.3	13.73	89.8	14.31
RH-34670	5.5	0.07	11.5	0.19	2.2	0.62	4.4	0.70
Met. A	1.2	0.02	1.5	0.03	-	-	-	-
Met. B	0.6	0.01	0.9	0.02	-	-	-	-
Met. C	-	-	-	-	ND	ND	0.7	0.11
H ₂ O- Sol	13.3	0.17	17.8	0.30				
Other Organosol.					2.3	0.33	5.1	0.81
PES	13.1	0.17	10.3	0.17	<0.1	<0.01	<0.1	<0.01
Identified	66.3	0.84	75.6	1.03	97.5	14.05	94.2	15.01
TRR	--	1.27	--	1.68	--	14.4	--	15.93

¹CPR = uniformly ¹⁴C-labeled in the chlorophenyl ring²NPR = uniformly ¹⁴C-labeled in the nitrophenyl ring³RH-34670 = 2-chloro-1-(3-hydroxy-4-nitrophenoxy)-4-(trifluoromethyl)-benzene⁴PES = Post-extraction solids